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TECH CENTER 1600/2900

Serial No.: 09/553,993  
Filed: April 20, 2000

PATENT  
Attorney Docket No.: A-69235/RMS/DCF

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:	)	
	)	
Gunderson et al.	)	Patent Examiner: Forman, B
	)	
Serial No.: 09/553,993	)	Group Art Unit: 1655
	)	
Filed: April 20, 2000	)	
	)	
For: DETECTION OF NUCLEIC	)	
<u>ACID REACTIONS ON BEAD ARRAYS</u>	)	

DECLARATION PURSUANT TO 37 C.F.R. § 1.132

Commissioner of Patents and Trademarks  
Washington, DC 20231

Sir:

I, John Stuelpnagel, do hereby declare as follows:

1. I received a B.S. in Biochemistry and a D.V.M. from the University of California, Davis, and a M.B.A. from the Anderson School at University of California, Los Angeles. A copy of my most recent Curriculum Vitae is provided as Attachment A, and forms a part hereof.

2. I am currently the Vice President of Business Development at Illumina, Inc. I have been employed at Illumina since its inception during which time I have managed the business development for the BeadArray™ detection technology. I have been intimately involved in the process of marketing the single nucleotide polymorphism (SNP) genotyping services, and with setting the specifications for the product. A copy of an advertisement of Illumina's SNP Genotyping services and technology is provided as Attachment B.

**Serial No.:** 09/553,993  
**Filed:** April 20, 2000

3. I am a co-inventor of the pending patent application U.S.S.N. 09/553,993. I have reviewed and I am familiar with: the specification and the claims of pending application U.S.S.N. 09/553,993; and the pending Office Action mailed November 27, 2001.

4. I have reviewed and am familiar with Barany (U.S. Patent No. 6,027,889, filed May 28, 1997) and Walt (U.S. Patent No. 6,023,540, filed March 14, 1997), the prior art references currently cited against this application.

5. Illumina's SNP Genotyping services have been and are currently sold to GlaxoSmithKline; Johns Hopkins Medical University, Institute of Genetic Medicine; Boston University Medical Center; Oxagen; and other undisclosed customers.

6. Illumina currently conducts genotyping assays by attaching an adapter nucleic acid to a target nucleic acid sequence to form a modified nucleic acid. The adapter nucleic acid hybridizes to specific captures probes, which are immobilized on a subpopulation of microspheres that are distributed at discrete sites on a patterned surface of a substrate. Detecting the hybridized modified nucleic acid on the microspheres allows detecting the presence of the target nucleic acid.

7. Illumina also conducts genotyping assays by hybridizing a primer comprising an adapter sequence to a portion of a target sequence. A second primer is hybridized to another portion of the target sequence, and the two hybridized primers are eventually ligated together to form a modified primer. The modified primer is hybridized to a specific capture probe that hybridizes to the adapter sequence. These capture probes are present on a subpopulation of microspheres, which are distributed at discrete sites on a substrate surface. Detecting the presence of a hybridized modified primer on the microsphere allows detecting the presence of the target nucleic acid.

## JOHN R. STUELPNAGEL

**Illumina, Inc.**  
9390 Towne Centre Drive, Suite 200  
San Diego, CA 92121  
858-587-4290, ext 226

P.O. Box 281  
Cardiff, CA 92007  
760-943-1541

### EXPERIENCE

#### **Illumina, Inc.**

VP Business Development and Director  
Acting President & CEO  
Acting CFO

San Diego, CA

*1998-present*

*1998-Oct. 1999*

*1998-Apr. 2000*

- Founded Illumina from technology licensed from Tufts University.
- Hired key scientific team, recruited Scientific Advisory Board, set initial product focus, acquired nGenetics, acquired Spyder Instruments, and determined the strategic direction of Company.
- Identified and recruited the permanent President & CEO.
- Raised \$38 million in private financing in three venture rounds and participated actively in \$100 million IPO.
- Negotiated and closed \$15 million joint development program with Applied Biosystems.
- Licensed additional intellectual property and established numerous research collaborations, including those with The Dow Chemical Company and Chevron.
- Guided the development of the intellectual property portfolio to include 15 issued patents and 50+ patent applications.
- Identified and negotiated real estate transactions, including the \$36 million purchase of the Company's corporate headquarters.

#### **CW Group**

Associate

Cardiff, CA

*1997-1998*

- Joined CW Group when CW Group acquired Catalyst Partners (see below).
- Responsible for identifying new investment opportunities and working with portfolio companies in business development.
- Founded Illumina for CW Group.
- Assisted the General Partners in raising \$100 million venture fund.

#### **Catalyst Partners/Avalon Ventures**

Principal

Cardiff, CA

*1996-1997*

- Identified and researched start-up opportunities in bioinformatics, chip olfaction, proteomics and acceleration of drug development.
- Founded bioinformatics company and negotiated its merger with another bioinformatics company, Pangea Systems. The combined company received \$10 million in venture financing.

Attachment  
A

• Worked with portfolio companies in business development:  
Caliper Technologies

- Performed financial analysis and worked on the team that negotiated strategic relationship with Hewlett-Packard valued in excess of \$100 million.
- Worked on team that negotiated strategic relationships with Hoffman-LaRoche and Dow Chemical valued in excess of \$30 million.
- Led licensing negotiations for key technologies, including the successful renegotiation of its core technology, reducing the royalty rate by 75%.
- Analyzed spin-out business opportunities, including ultra-high throughput drug screening and pharmacogenetics.

IDUN Pharmaceuticals

- Licensed key technologies.

**InnoCal, Venture Capital**  
Intern

Costa Mesa, CA  
Summer, 1996

- Researched the health care information industry to identify investment opportunities.
- Evaluated combinatorial chemistry companies in support of an acquisition offer.
- Analyzed the veterinary market for a portfolio company developing a human pharmaceutical.

**Keystone Biomedical, Inc.**  
Consultant

Los Angeles, CA  
1995-1996

- Assisted in the founding of biotechnology.
- Authored business plan used in obtaining \$1.2 million in seed capital.

**Veterinary Practice**  
Veterinarian

Santa Barbara and Santa Ynez, CA  
1983-1996

## EDUCATION

**M.B.A., The Anderson School at UCLA**  
Awards and Honors

1997

Henry Ford II Fellowship to top student  
Edward W. Carter Fellowship to top 2% of class  
Venture Fellowship  
Dean's Fellowship  
Director, Entrepreneurs Association

**D.V.M., School of Veterinary Medicine, UC Davis**  
Awards and Honors

1983

Valedictorian, School Medalist

University of California Regents Scholar  
CVMA Award for Practice Excellence  
Merck Award  
Phi Zeta Honor Society, President

**B.S., College of Agriculture, UC Davis**  
Awards and Honors

1979

Valedictorian, College Medalist  
Research

Etiology, Biochemistry and Diagnosis of Degenerative Joint Disease

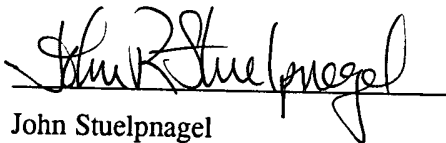
Serial No.: 09/553,993  
Filed: April 20, 2000

8. Illumina's SNP Genotyping services are commercially successful. After marketing began in June of 2001, Illumina has secured six genotyping contracts from pharmaceutical and biotechnology companies, and major academic institutions. The genotyping services have substantially increased its capacity to over one million genotypes per day. The servicing agreements generate substantial revenue for Illumina; there has been substantial growth in service agreements, which is expected to further increase in 2002. Copies of news releases pertaining to the commercial agreements are provided as Attachment C.

9. The commercial success of Illumina technology is directly related to the BeadArray™ nucleic acid detection system using microspheres and the multiplexed assay formats developed at Illumina. In my opinion, the system's high throughput, cost effectiveness, accuracy, and flexibility, as embodied in claims 1 and 14 are directly responsible for its commercial success.

10. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that the making of willful, false statements, and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that such willful statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 4/25/02

  
John Stuelpnagel  
Vice President, Business Development

# Illumina's SNP Genotyping Services and Technology

How Illumina's BeadArray™ platform and an advanced LIMS environment provide high throughput, accuracy and low genotyping cost.

## INTRODUCTION

Illumina has developed SNP genotyping services that leverage highly multiplexed and automated assays processed on our BeadArray™ platform. Illumina's system delivers superior performance, throughput, cost-effectiveness and accuracy to researchers interested in large-scale genotyping.

With a capacity approaching one million genotypes per day, Illumina's scientific operation integrates a high degree of automation with an advanced laboratory information management system (LIMS) for error-free sample tracking.

Illumina's high throughput genotyping services will enable linkage analysis, fine mapping of selected chromosomal regions, identification of candidate gene SNPs, and large association studies.

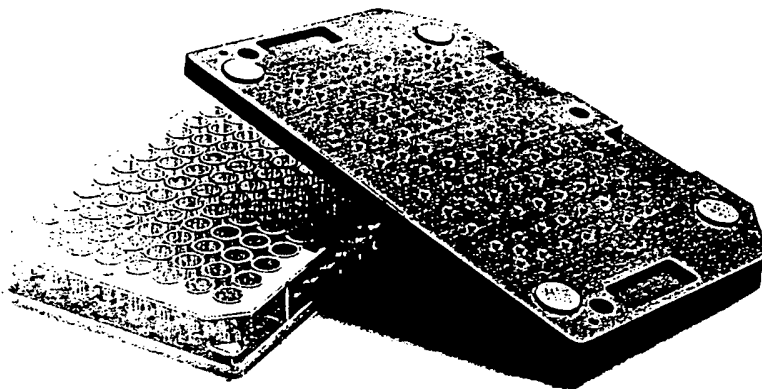
## GENOTYPING SERVICES MENU

Custom assay development and genotyping

SNPs in Drug Metabolizing Enzymes (≥ 175 ADME-changing loci)

Linkage Sets (targeted delivery Q4 '01)

Disequilibrium Set (targeted delivery Q2 '02)



Illumina's 96-bundle Array of Arrays enables parallel processing of nearly 200,000 SNPs.

## BEADARRAY™ TECHNOLOGY

At the heart of Illumina's platform is our BeadArray technology—a fiber optic-based array system that allows miniaturized, very-high-throughput genetic analysis.

In our current implementation, fiber bundles are manufactured to contain nearly 50,000 individual, light-transmitting fiber strands. We convert each fiber bundle into an array by first chemically etching a microscopic well at the end of each fiber strand within a bundle. This process creates up to 50,000 discrete microscopic wells per bundle.

In a separate process, we create sensors by affixing a specific type of molecule to beads, each bead approximately 3-microns in diameter, in high quality-controlled batches. The particular molecules on a bead define that bead's function as a sensor. For example, we create a batch of SNP sensors by attaching

a particular DNA sequence to each bead in a batch. We then combine these batches of coated beads to form a pool specific to the type of array we intend to create. In the case of our SNP genotyping product, the array pool we have selected uses DNA sequences that do not cross-hybridize with themselves or with known genomic DNA.

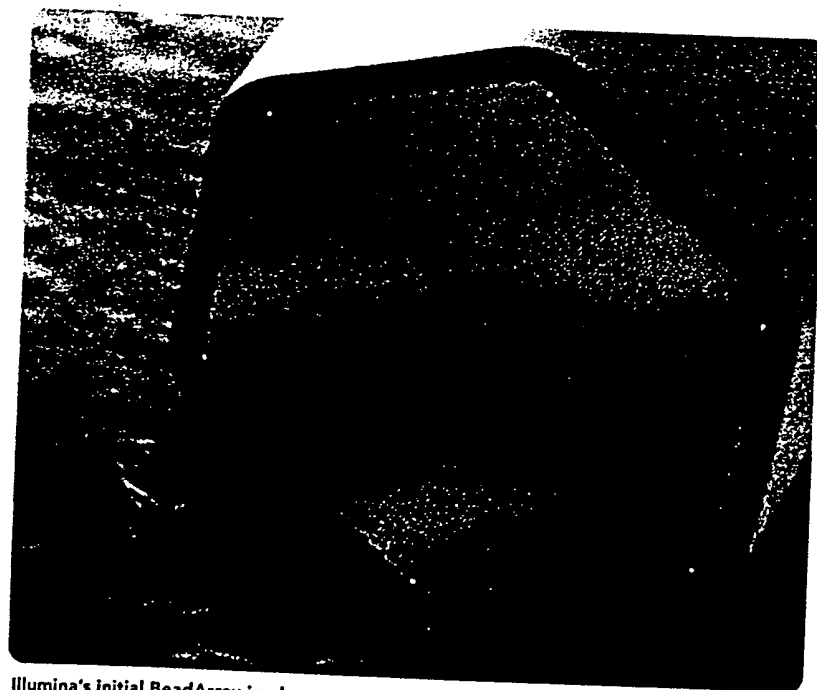
The next step in the manufacturing process involves creating the self-assembled array. By dipping the bundles into a pre-mixed bead pool the coated beads self-assemble individually, one bead per well, on the end of each fiber in the bundle to create the array. In our SNP genotyping array, the bead pool consists of up to 2000 unique sequences. These 2000 unique SNP sensor beads self assemble in each bundle of 50,000 fibers to create an array with an approximately twenty-five-fold redundancy. This built-in

redundancy improves the reliability and accuracy of the results generated by the BeadArray technology.

Illumina further fabricates its BeadArray bundles into a matrixed device, which we call our Array of Arrays™ platform, where each fiber bundle of the larger array matches a well of a standard microtiter plate. In the 96 well configuration and at 2000 bead types per array bundle, this Array of Arrays format would enable up to 192,000 individual genotypes to be scored in parallel.

#### Built-In Quality Control

Following array assembly and as a component of our manufacturing process, we deploy a proprietary decoding process to determine which bead type resides in which fiber core. Beyond generating a map that is used in downstream analytical work, our decoding process delivers inherent quality control as it validates the performance of each bead on each array.



Illumina's initial BeadArray implementation contains approximately 50,000 beads in individual 3-micron wells at the end of each fiber strand.

With our Oligator™ custom DNA synthesis technology, Illumina also manufactures the oligonucleotides used in our BeadArray products, thus controlling the quality and supply of the oligonucleotides used in our BeadArray products and in SNP genotyping services.

#### KEY ADVANTAGES OF ILLUMINA'S TECHNOLOGY

**Throughput:** Miniaturization, multiplexing and automation drive throughput.

**Cost Effectiveness:** Proprietary manufacturing process provides low cost structure.

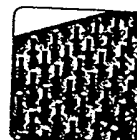
**Accuracy:** Decoding performs a quality control step for every feature on every array. Redundancy provides robustness and improves data quality.

**Flexibility:** Various shapes, sizes and configurations of fiber bundles with choices of bead chemistry results in a flexible platform.

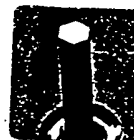
#### BeadArray Technology How it works



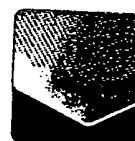
1 Compatible with manual or robotic operation, our Array of Arrays format is designed to match the wells of standard microtiter plates.



2 Close up of the bead-containing ends of the fiber bundles arrayed in a 96-well format.



3 Dipping the fiber optic bundle into a chemical solution etches a microscopic well at the end of each individual fiber in the bundle.



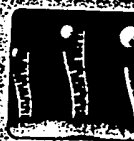
4 To form an array, we dip each fiber bundle into a pool of coated beads which self-assemble into the wells, one bead per well.



5 Up to 2000 different bead types, with each bead type containing oligonucleotides of a unique sequence, can be represented in each bundle, with a targeted twenty five-fold average redundancy per bead type.



6 Hundreds of thousands of molecules of the same type coat each bead. We determine which bead type occupies which well via a proprietary decoding process.



7 The molecules in the sample hybridize, or bind to their complementary molecules on the coated bead.



#### LIMS ENVIRONMENT

Illumina has enabled its BeadArray technology with a state-of-the-art laboratory information management system (LIMS) to create an ultra-high-throughput genotyping service operation.

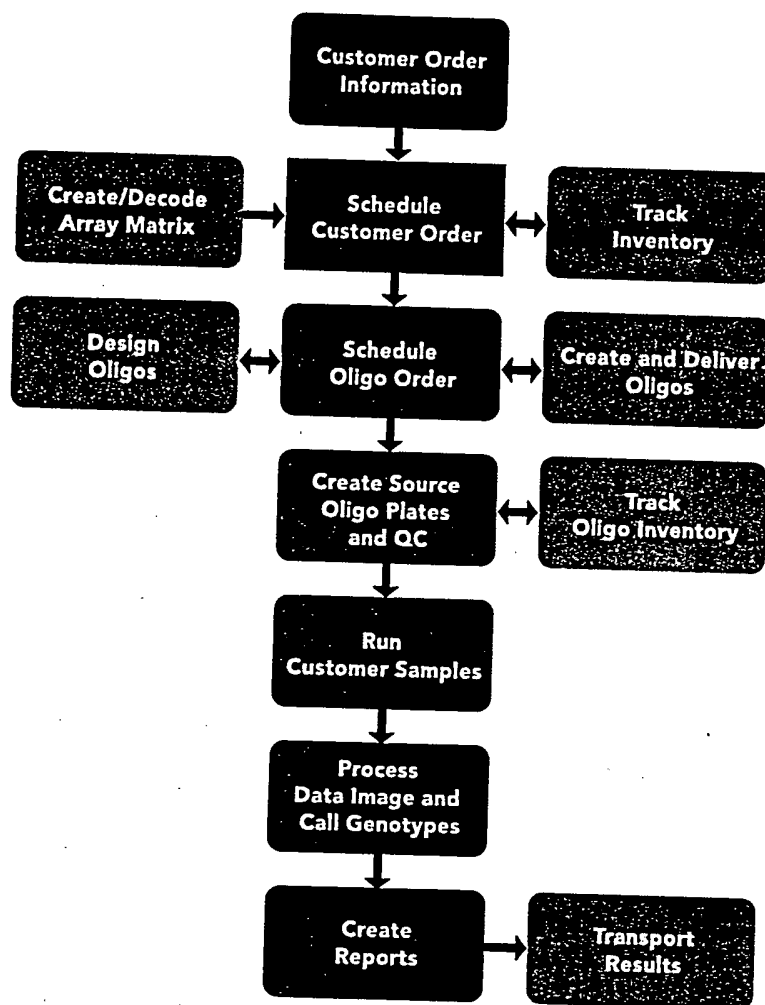
The LIMS environment was created as a customized database system for the workflow tracking and management in our genotyping facility. Every sample is given a unique identifier in the LIMS that links the genotyping order with specific reagents, microtiter plates and oligos. This allows the LIMS database to actively monitor all operations and ensure error free sample processing.

Our genotyping facility is designed to grow with customer needs and business demands. We have modularized our automated system to eliminate bottlenecks without sacrificing flexibility and cost. If more upfront sample processing is required, we simply install additional sample processing modules without affecting any downstream genotyping processes. This allows us to scale effortlessly while maintaining the strict rigor of sample handling and control.

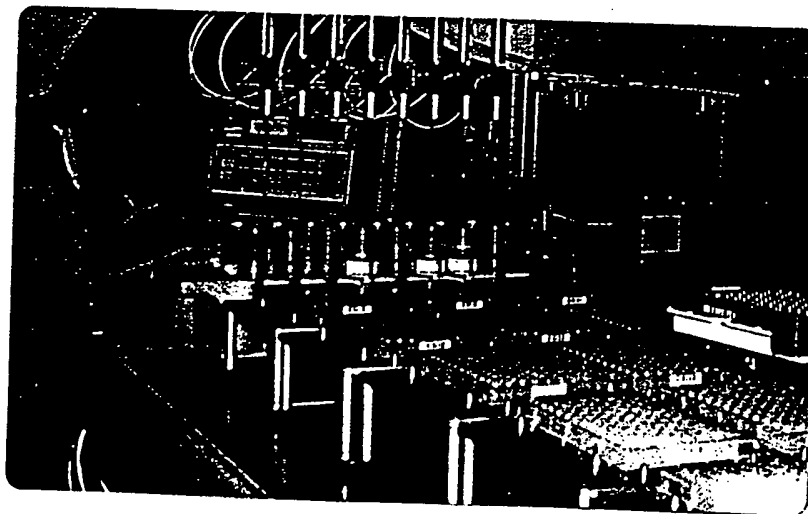
#### HOW WE WORK WITH YOU

Illumina has assembled an experienced team of scientific professionals to deploy BeadArray technology in an automated, LIMS-controlled production environment. We take a highly collaborative approach to our customer relationships, maintaining strict confidentiality while pursuing ongoing dialogue to ensure productive results.

To get started, we will first test samples of your anonymized DNA for assay compatibility prior to the initiation of a genotyping project.



Simplified flow diagram of Illumina's SNP genotyping service, which is automated and LIMS-enabled at every step of the process.



We will then provide you with bar-coded plates for shipment of samples to Illumina, followed up by quality-control checks on each sample. Only then will we begin the study. The amount of genomic DNA required by a study will be determined by the number of SNP loci analyzed for each sample. To calculate the amount of genomic DNA required for a sample, please contact Illumina or see our Frequently Asked Questions brochure available on our website.

For your study, we encourage a collaborative approach to designing the study and selecting the SNP loci. We can validate the loci for you and will convert those loci into functional assays.

ACCURACY (STRAND CORRELATION)*	
Study Set	% Accuracy
1	98.9
2	99.3
3	99.4
4	99.7

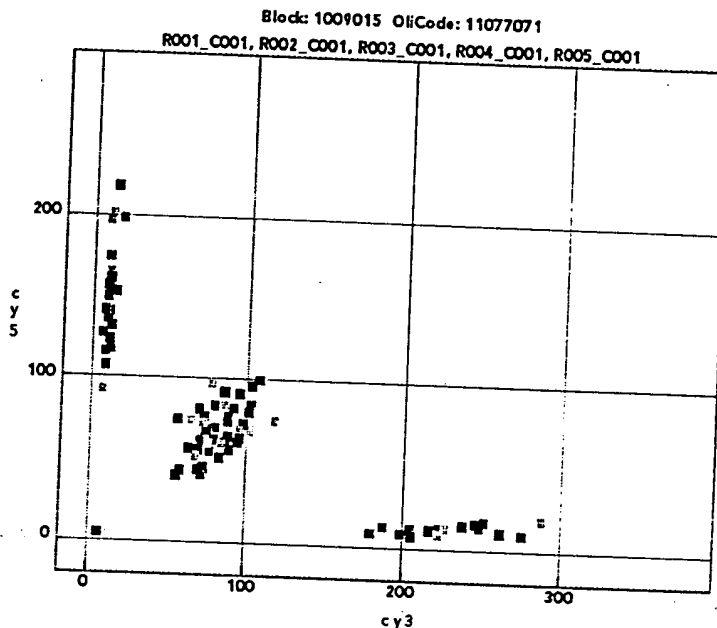
\* This chart represents results generated from four sets of Loci (approximately 100 loci in each set) from 55,912 Alleles at a 90% call rate.

#### MORE INFORMATION

To learn more about Illumina's SNP genotyping services, BeadArray technology, Oligator custom DNA synthesis services, or other products and services, please visit our website or contact us at the address below.

Note: Please visit our website for the most recent version of this document.

#### GENOTYPING CLUSTERING: 1 LOCUS FROM A 96 MULTIPLEXED LOCI SET WITH 96 DNA SAMPLES



Illumina, Inc.  
9885 Towne Centre Drive  
San Diego, CA 92121-1975  
tel 1.858.202.4500  
fax 1.858.202.4545  
www.illumina.com

# Enter the New World

Welcome to the new world.

A world where genotyping studies can be conducted with speed, sample throughput, and scale never before possible.

At a lower cost than you ever imagined. Large studies that once took years can now be completed in months or even days.

With a throughput level of 1,000,000 calls per day,

Illumina's SNP genotyping service leverages our proprietary BeadArray™

technology. The BeadArray platform will be available as a product later this year, but you can access its remarkable benefits now through our new genotyping service.

Illumina's service operation integrates a high degree of automation with advanced LIMS to manage linkage analyses, fine chromosomal mapping, candidate gene and large association studies.

So expand your expectations. Readjust your planning calendar. And join us in the new world of genotyping.

Learn more by calling us at 1.800.809.4566 or visiting [www.illumina.com/1snp](http://www.illumina.com/1snp)

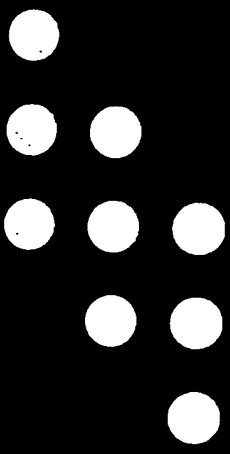
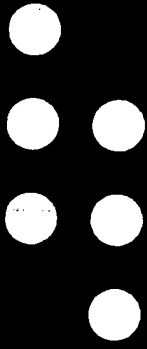


Illumina's BeadArray™ technology allows parallel processing of over 150,000 SNPs.

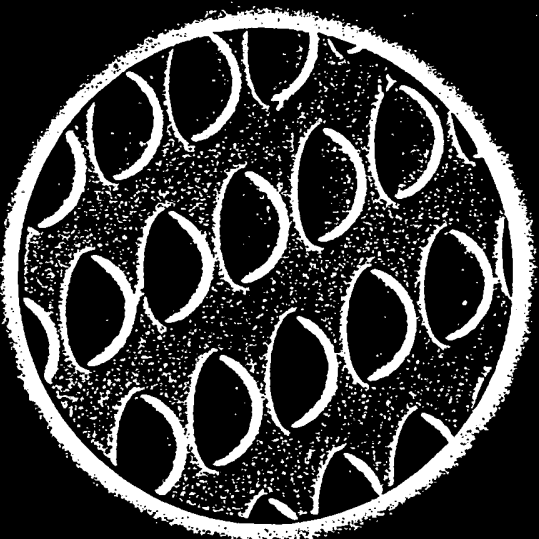
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**illumina.**  
making sense out of life

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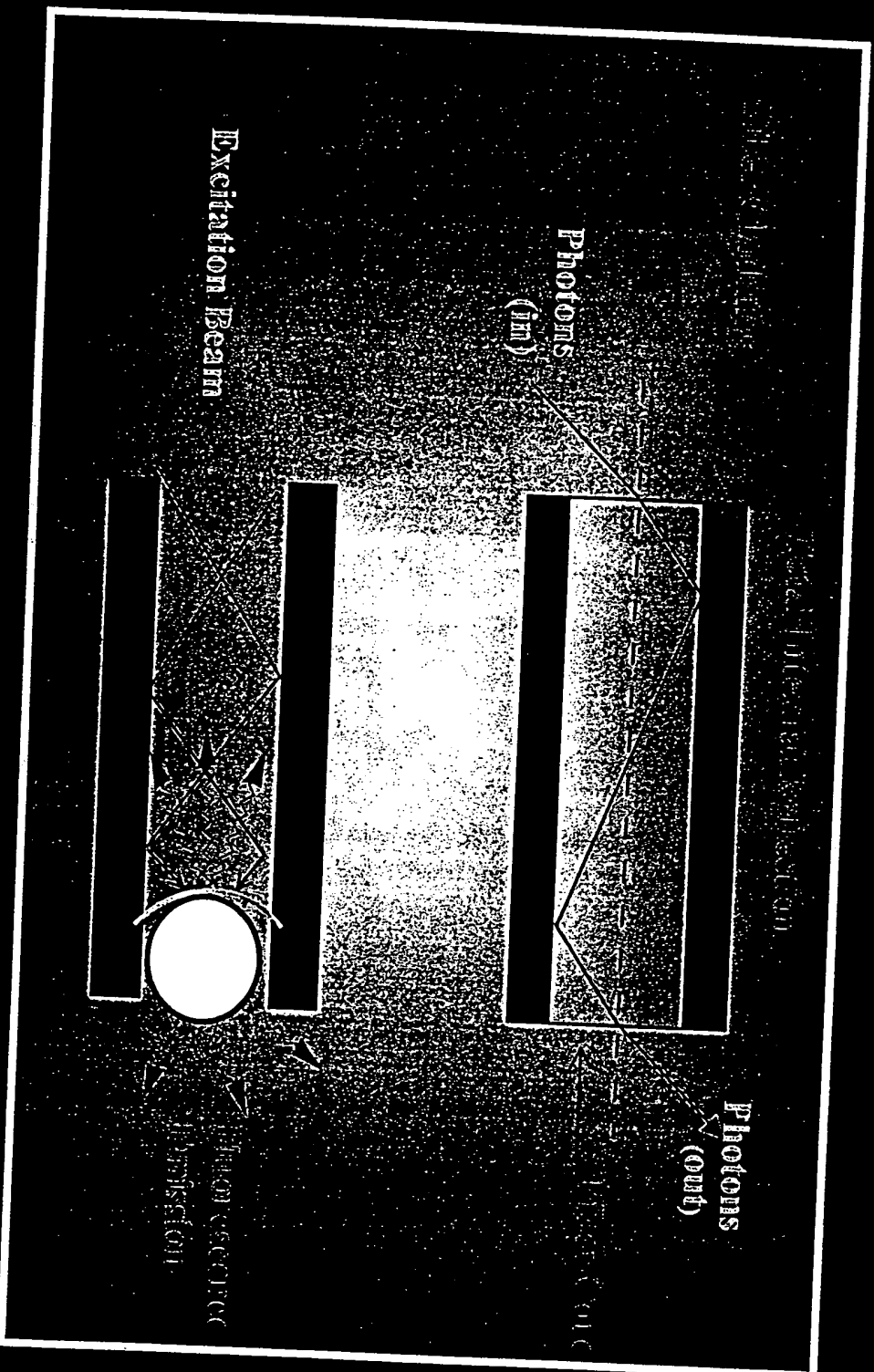
# **Illumina's Revolutionary Technology: Bringing Fiber Optics to Biology**



- **Throughput**
- **Cost-effectiveness**
- **Accuracy**
- **Flexibility**

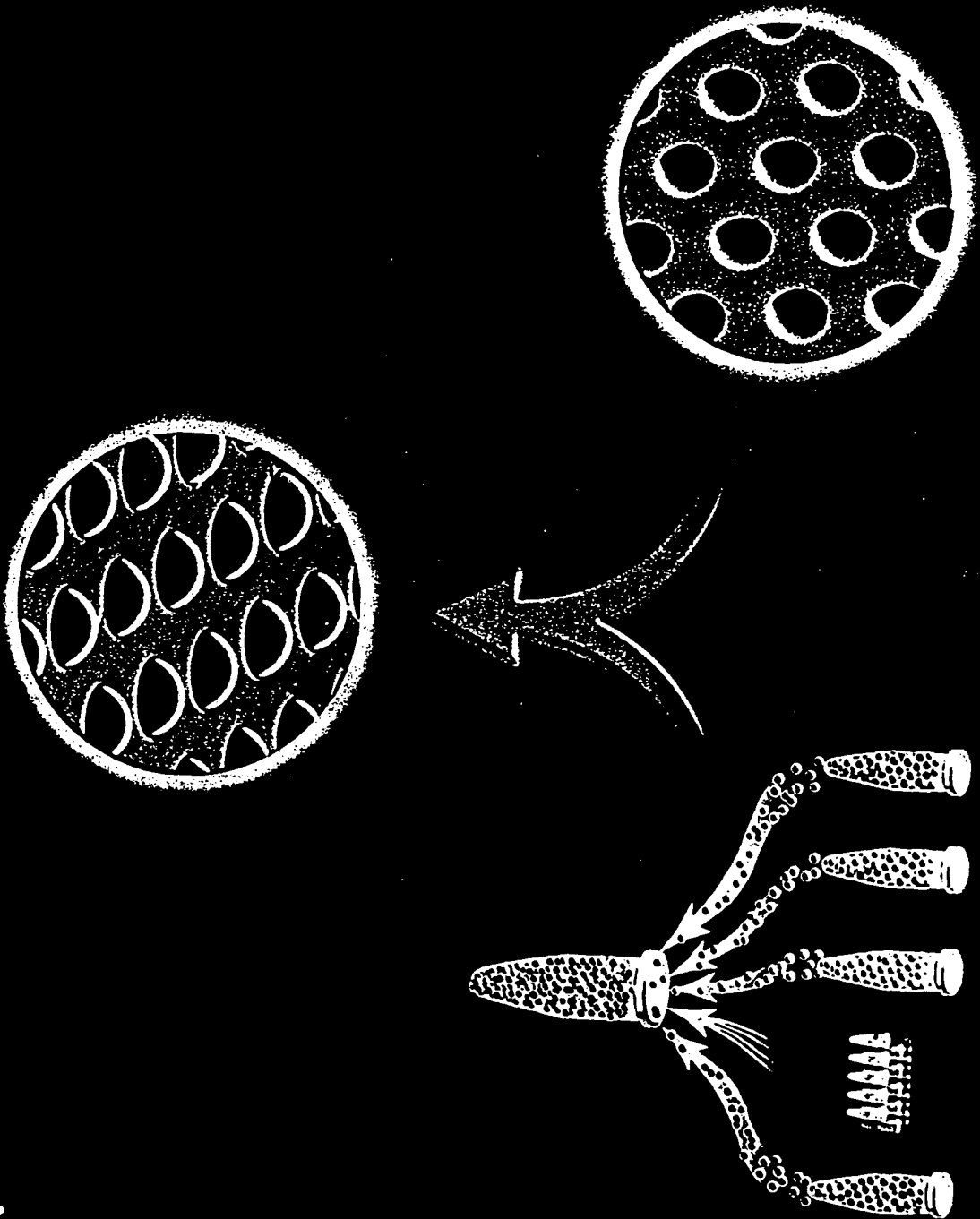
**illumina**

# Bringing Fiber Optics to Biology



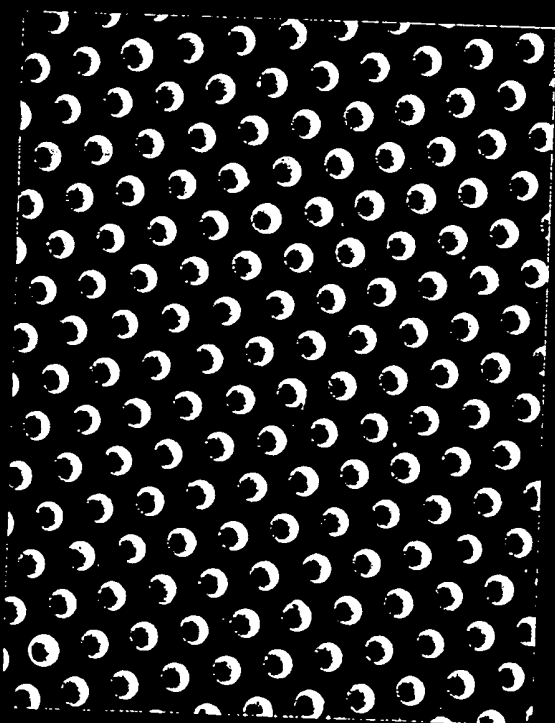
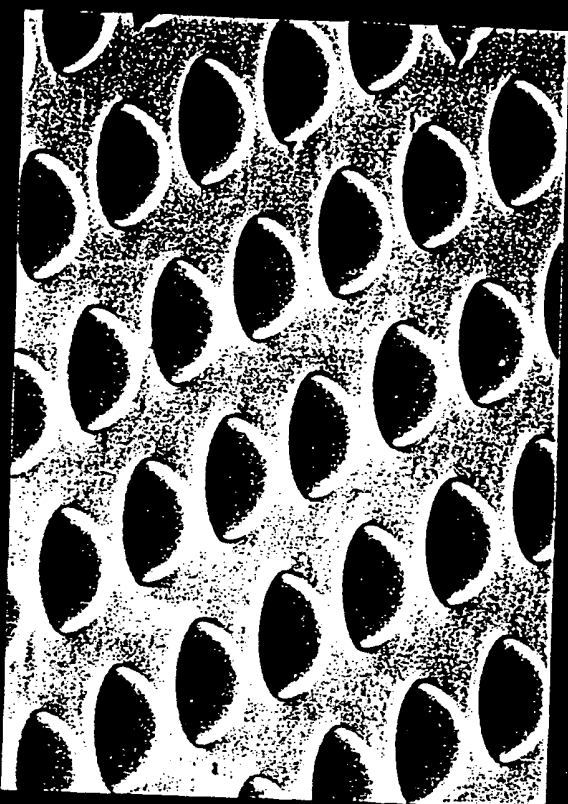
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# The BeadArray™ Assembly Process



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# **“Optically Wired” Beads in Wells**



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# Random Bead Arrays Require Decoding

- Standard arrays are “ordered”
  - Each element is manufactured in a known place
    - Robotic spotting
    - Photolithography
    - Ink jet synthesis
- Illumina Bead Arrays are “random”
  - Manufactured by self-assembly
  - Beads are identified by decoding

# Fiber Bundles: A Flexible Platform



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# Illumina's Technology Advantages

- **Throughput:** Miniaturization yields greater informational density than any other format and product formats are compatible with conventional automation.
- **Cost-effectiveness:** Proprietary manufacturing process provides low cost structure.
- **Accuracy:** Decoding performs a quality control step for every feature on every array and multiple bead types improves data quality.
- **Flexibility:** Various shapes, sizes and configurations of fiber bundles with choices of bead chemistry results in a flexible platform.

# Commercialization Model

Technology

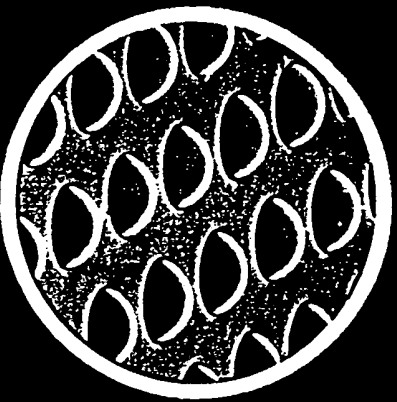
Performance

Applications

Assay

Development

Commercialization



BeadArray™



Oligator™

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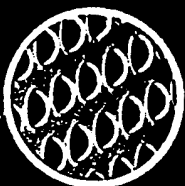
# Commercialization Model

Technology

Platforms

Applications

BeadArray™



Oligator™



1536-Well



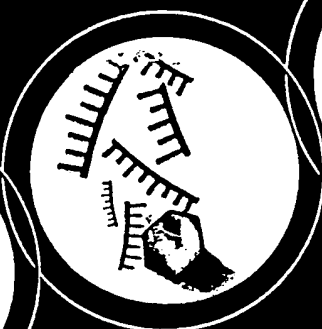
384-Well



96-Well



SNP Genotyping



Expression  
Profiling



Proteomics

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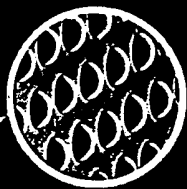
# Commercialization Model

Technology

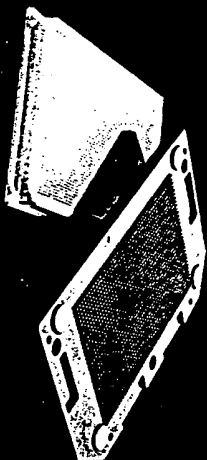
Platforms

Application

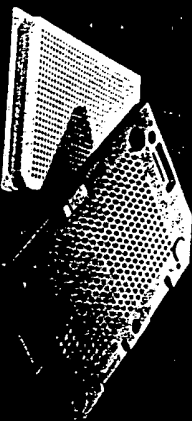
BeadArray™



Oligator™



1536-Well  
3,072,000 Assays



384-Well  
768,000 Assays



96-Well  
192,000 Assays

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# Commercialization Model

Technology

Platforms

Applications

BeadArray™



Oligator™



1536-Well



384-Well



96-Well



SNP Genotyping



Expression Profiling



Proteomics

Assay Development

Custom Assays

- "Customer Favorites"
- 100-1000 SNPs

Linkage

- Candidate Genes
- 1K-5K SNPs

Linkage Disequilibrium

- Whole-Genome Scans
- 100K-200K SNPs

Focused Sets

- 1K-10K Genes
  - Lots of Samples
- Whole Genomes

Antibodies

Alternative Capture Molecules

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# Commercialization Model

Technology

Platforms

Applications

Assay Development

Commercialization

Services Products

Oligos

ABI Partnership

Direct Sales

BeadArray™

Oligator™



1536-Well



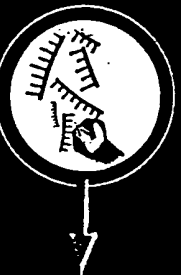
384-Well



96-Well



SNP Genotyping



Expression Profiling



Proteomics

- Custom Assays
- Linkage
- Linkage Disequilibrium

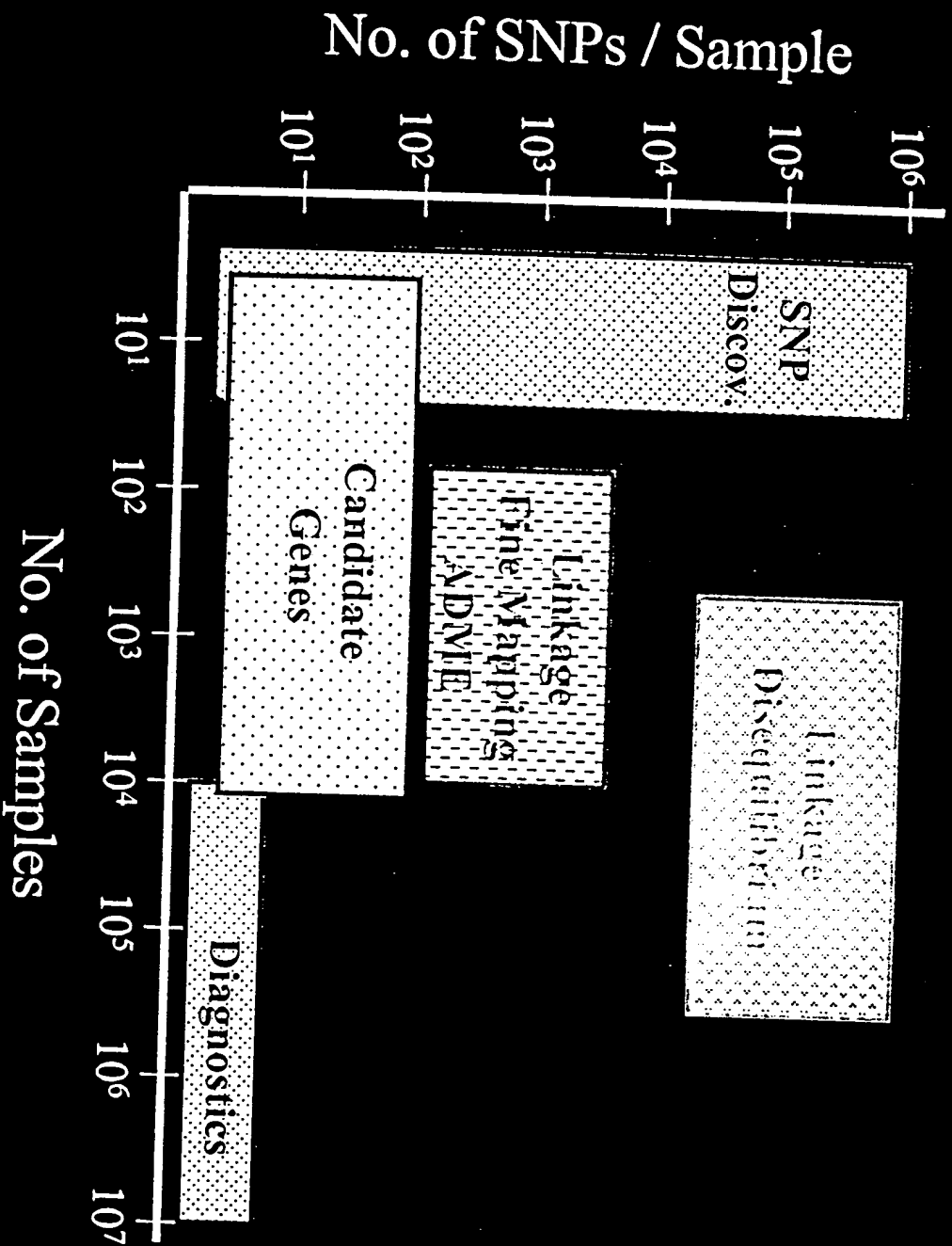
- Focused Sets
- Whole Genomes
- Antibodies
- Alternative Capture Molecules



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# SNP Market Segmentation

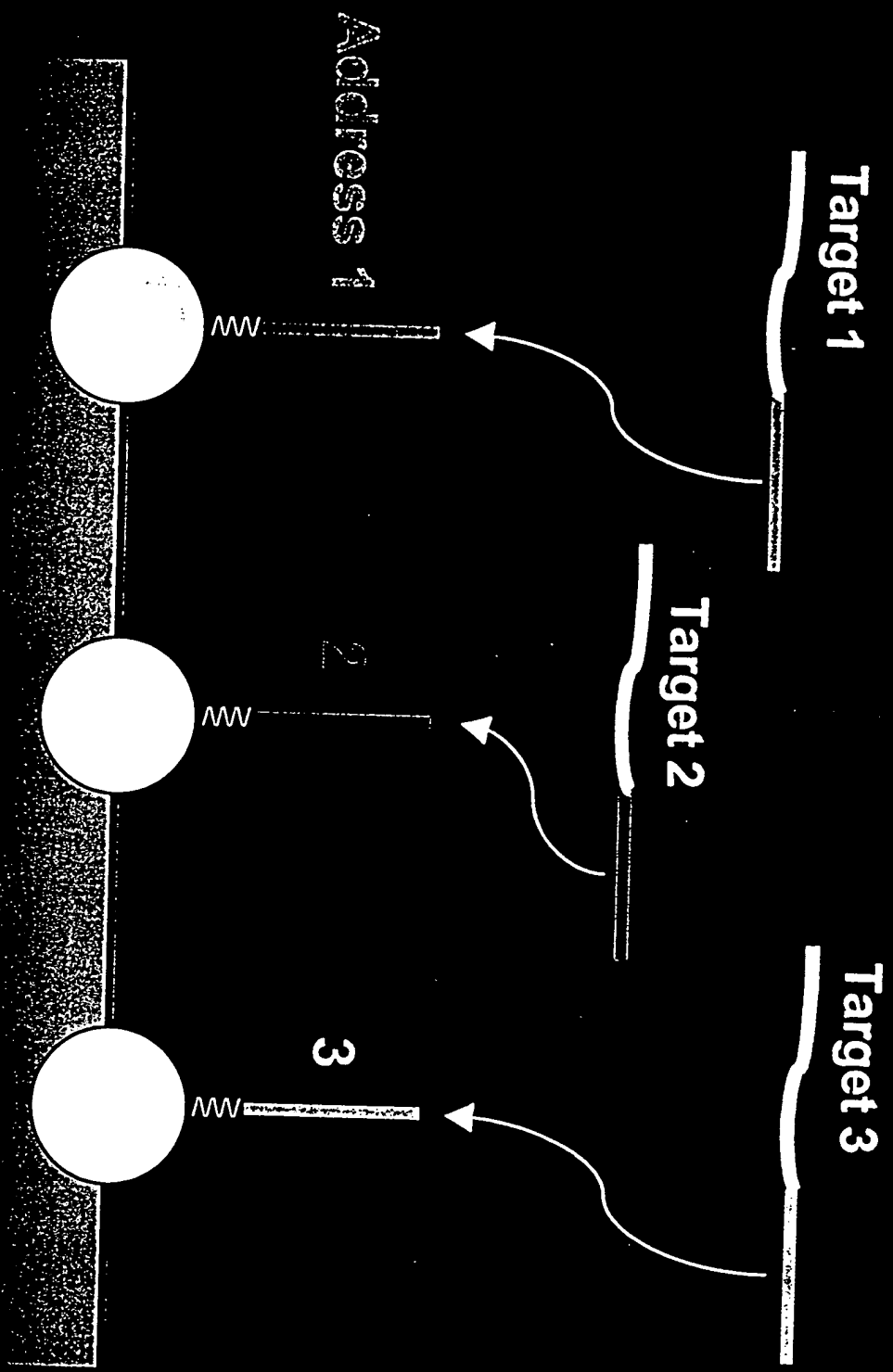


# Some Dimensions of Genotyping

## Assay

- Production System
- Quality metrics/Controls
- DNAs
- Loci
- Production/Data
- Summary/Plans/Capacity

# Universal Arrays



# **Optimization of the Assay**

## **Ligation**

- Buffer composition
- Temperature, Time
- Enzyme concentration
- Concentrations of gDNA, oligos

## **PCR Amplification**

- Primer sequences
- Cycle Profile
- Uniformity

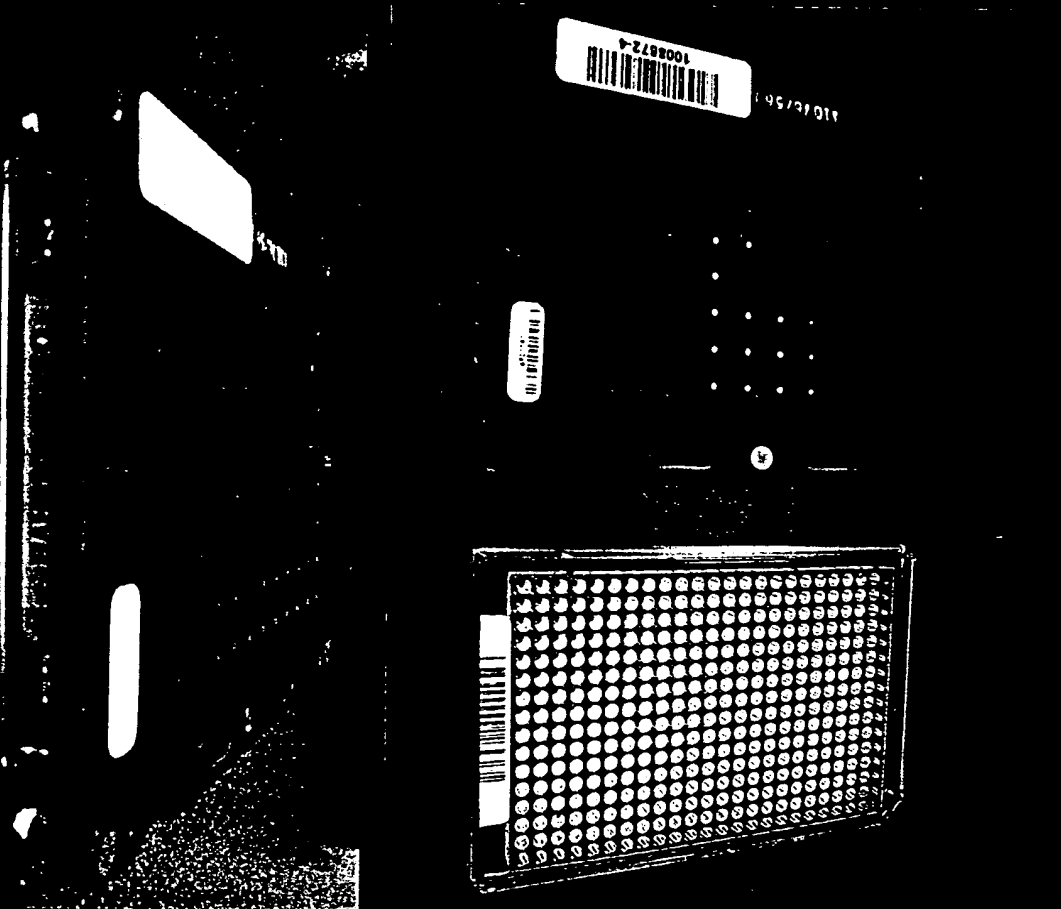
## **Hybridization to Array**

- Buffer composition
- ss-DNA vs. ds-DNA

## **Imaging**

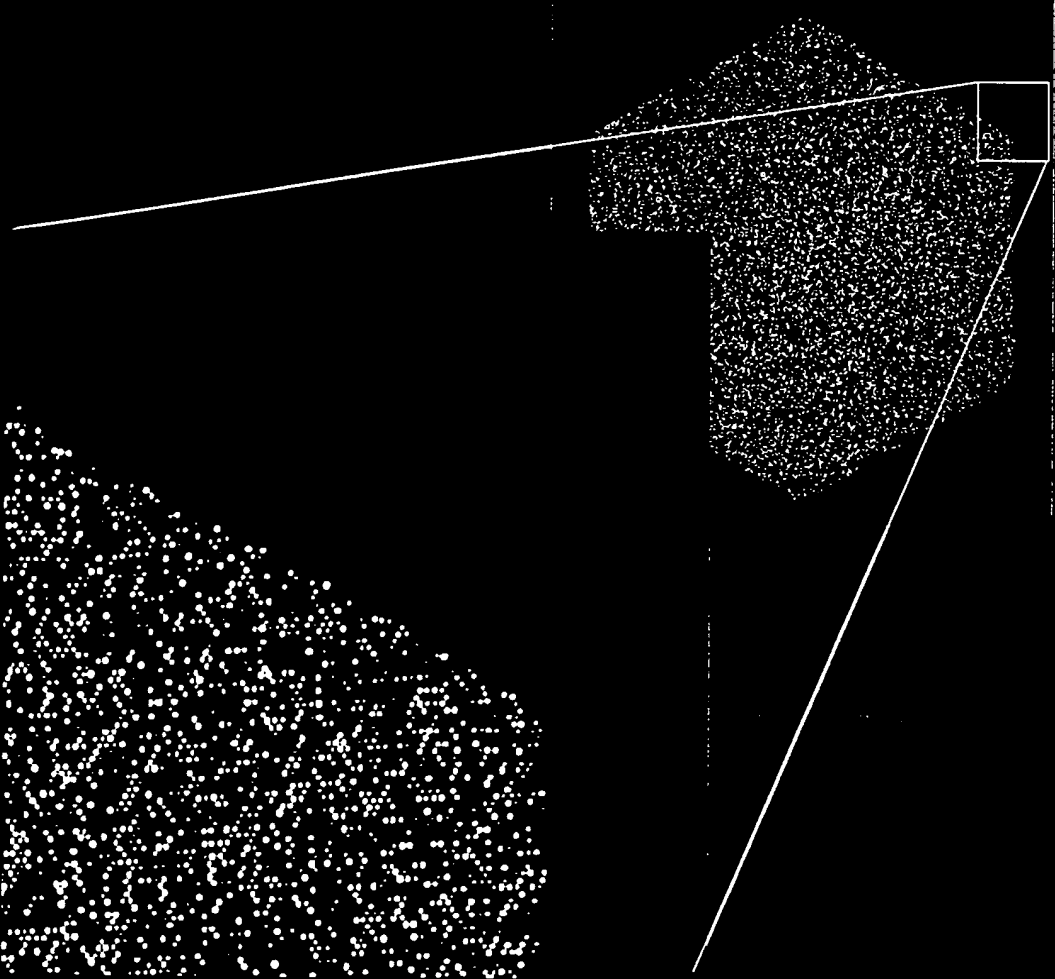
- Buffer composition
- Equipment, Software

# Hybridization



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# Hybridization Image



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# Some Dimensions of Genotyping

- o Assay
- o Production System
- o Quality metrics/Controls
- o DNAs
- o Loci
- o Production/Data
- o Summary/Plans/Capacity

# Genotyping Service Facility

## Resources

- 5 Tecan Robots
- 5 People
- 3 Thermal Cyclers
- 4 Ovens
- 2 Array Readers

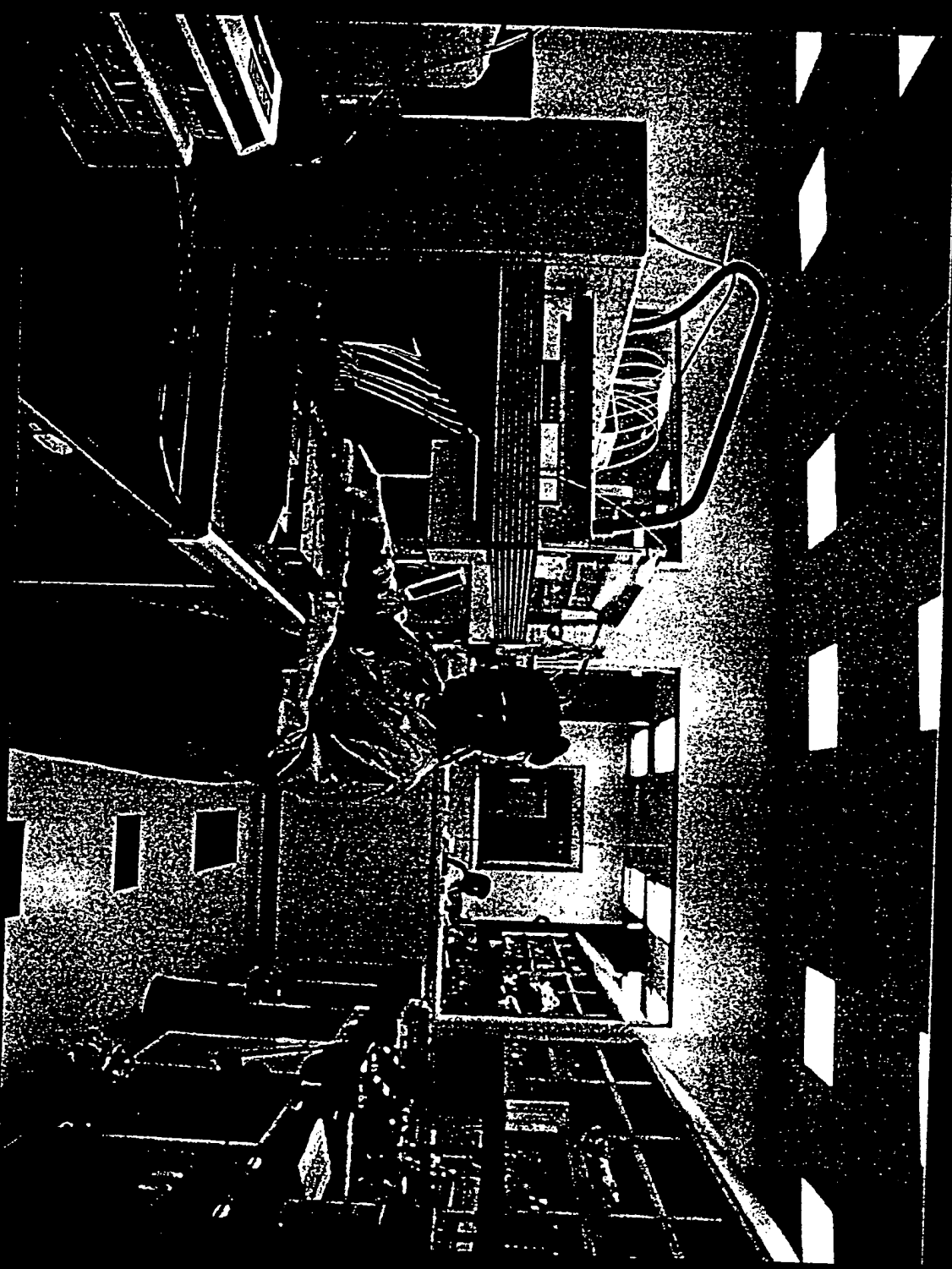
## Capacity

- ~1,000,000

Genotypes / Day

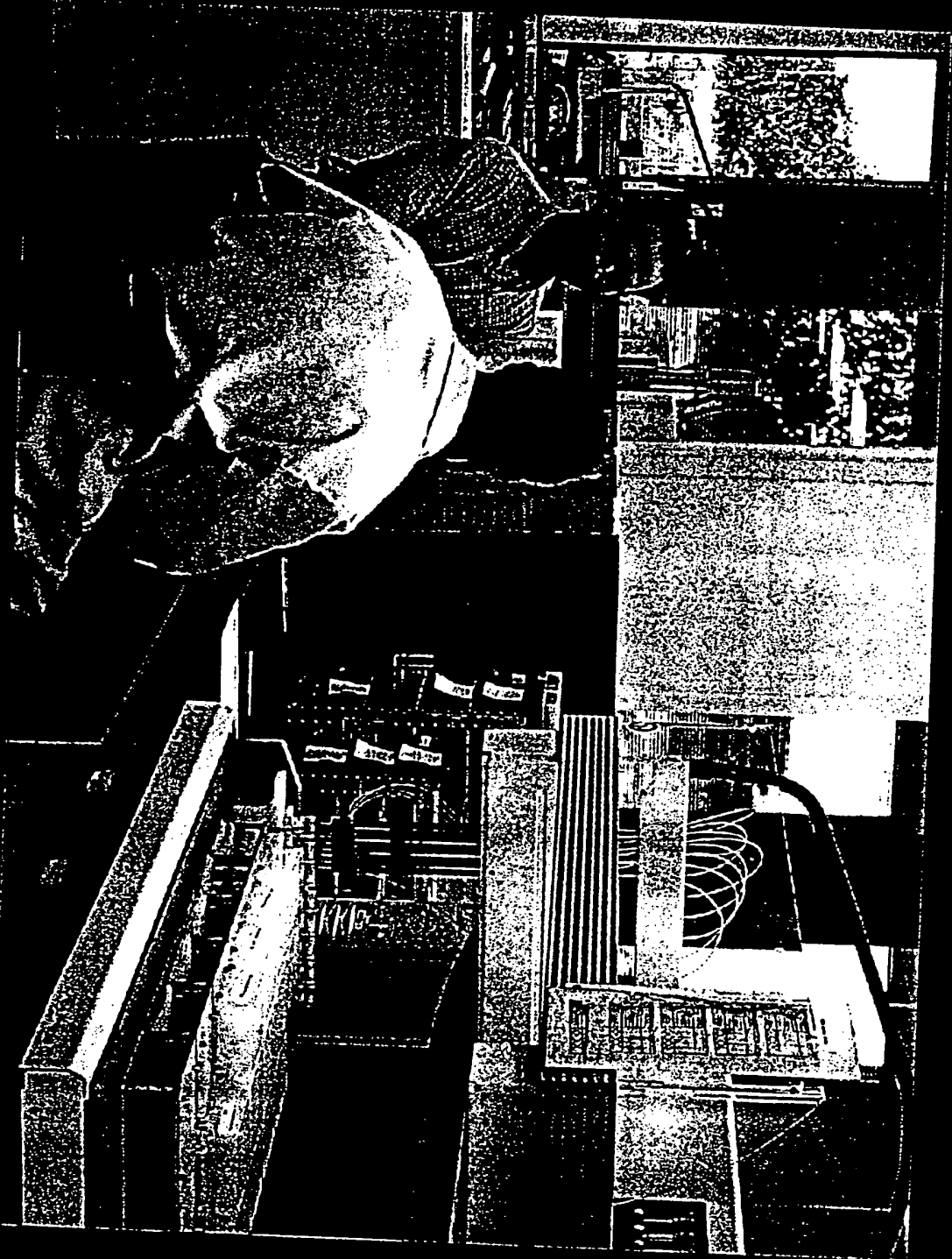


# Pre-PCR Room



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# Post-PCR Lab



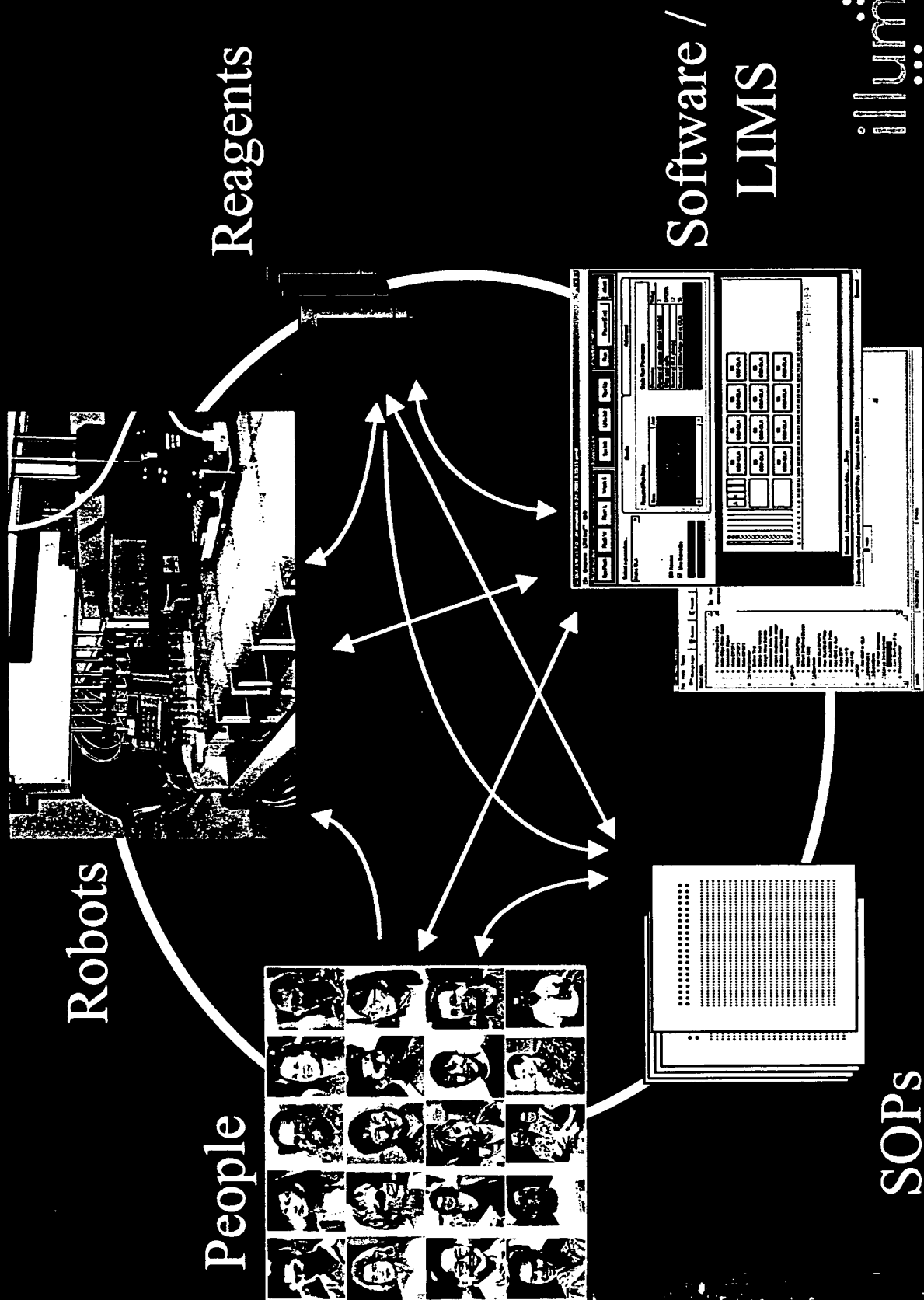
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# Array Readers



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# Integrated System for Genotyping



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# Automation Principles

- Custom LIMS Design
  - Fail-safe sample tracking
  - Experience with clinical sample tracking
- Modular robotics
  - Scalable
  - Fast Development Time
- Coordination with assay development
  - A common language for defining processes

# Some Dimensions of Genotyping

Assay

Production System

Quality metrics/Controls

DNAs / Loci

Productivity/Output

Scalability/Throughput

illumina

# Estimates of Accuracy

- Strand Correlation
  - Loci developed on both strands
  - Assumes strand independence in locus development
- Reproducibility
  - Duplicated DNAs
  - Assumes equivalence of DNAs

# Some Dimensions of Genotyping

Assay

Production System

Quality metrics/Controls

DNAs

LocI

Production/Data

Storage/Portability



# **Locus Development Success Factors**

- Allele frequency & source of allelic DNA
- Repeated sequences around polymorphism
- Palindromic sequences
- GC & AT rich sequences
- Neighboring polymorphisms
- Reagent variables (oligos)



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## news releases

### Illumina Signs Genotyping Services Agreement with GlaxoSmithKline

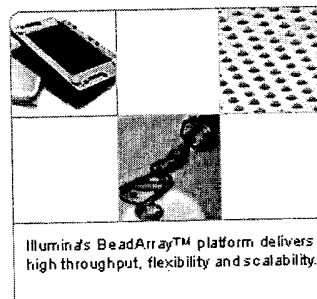
#### *SNP Scoring Service to Leverage Illumina's BeadArray Platform Technology*

SAN DIEGO, CALIFORNIA, June 29, 2001 -- Illumina, Inc. announced today that it has signed a commercial agreement with GlaxoSmithKline (GSK) to provide single nucleotide polymorphism (SNP) genotyping services on a sample collection provided by GSK. Under the terms of the agreement, Illumina will use its BeadArray technology to "score," or determine the frequency of specified SNPs in the sample set. Further details were not disclosed.

"We're pleased to begin working with GlaxoSmithKline, a global pharmaceutical firm and leader in employing new technologies to accelerate drug discovery," stated Jay Flatley, Illumina President and CEO. "Commercialization of our genetic analysis services business will drive the scale-up of genotyping assay development and help us refine BeadArray core technologies," added Flatley.

Illumina (Nasdaq: ILMN; [www.illumina.com](http://www.illumina.com)) is developing next-generation tools that will permit large-scale analysis of genetic variation and function. The Company's proprietary BeadArray<sup>®</sup> technology will provide the throughput, cost effectiveness and flexibility necessary to enable researchers in the life sciences and pharmaceutical industries to perform the billions of tests necessary to extract medically valuable information from advances in genomics. Illumina's technology will have applicability across a wide variety of industries beyond life sciences and pharmaceuticals, including agriculture, food, chemicals and petrochemicals.

Statements included in this press release that are not historical in nature may be "forward




Illumina's BeadArray<sup>™</sup> platform delivers high throughput, flexibility and scalability.

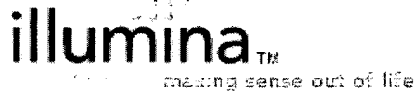
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Attachment  
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are not historical in nature may be forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Examples of such forward-looking statements include statements about Illumina's product introduction timeline or the Company's ability to further commercialize its genetic analysis services business or develop its core technologies. Any such forward-looking statements involve risks and uncertainties and reflect Illumina's judgment as of the date of this release. Actual events or results may differ from Illumina's expectations as a result of risks and uncertainties identified from time to time in the Company's reports filed with the U.S. Securities and Exchange Commission, including those discussed in "Factors Affecting Our Operating Results" and elsewhere in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2000 or in information disclosed in public conference calls, the date and time of which are released beforehand. Illumina disclaims any intent or obligation to update these forward-looking statements beyond the date of this release and claims the protection of the Safe Harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

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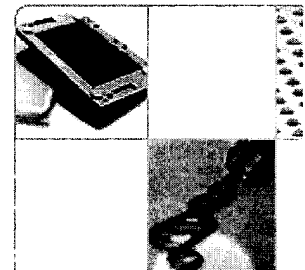
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**news releases****Illumina Signs Genotyping Services Agreement with University of California, San Diego and San Diego VA Healthcare System*****BeadArray(TM) Technology To Help Correlate SNP Genotypes with Bipolar Psychiatric Disorders***

SAN DIEGO, CALIFORNIA, April 25, 2002 -- Illumina, Inc. announced today that it has signed a commercial agreement with the University of California, San Diego (UCSD), to provide single nucleotide polymorphism (SNP) genotyping services on a sample collection provided by the University's Laboratory of Psychiatric Genomics. Under the terms of the agreement, Illumina will use its BeadArray technology to genotype specified SNPs in the sample set. Illumina will also identify potential SNPs for the study and design functional assays for the SNP loci, many of which are located on chromosome 22 and believed to be associated with bipolar disorders and schizophrenia. The study will be funded by a grant from the Department of Veterans Affairs. Further details about the agreement were not disclosed.

Jay Flatley, Illumina President & CEO, noted "UCSD is increasingly at the forefront of groundbreaking research in the field of psychiatry. We're very pleased to work with UCSD on this study, the results of which may provide a better understanding of the genetic basis of bipolar psychiatric disorders and suggest a clearer path for therapeutic development and improved patient outcomes. We're also excited to see further deployment of BeadArray technology in our services operation."

Illumina (Nasdaq: ILMN; [www.illumina.com](http://www.illumina.com)) is developing next-generation tools that permit large-scale analysis of genetic variation and function. The Company's proprietary BeadArray<sup>®</sup> technology provides the throughput, cost effectiveness and flexibility necessary to enable researchers in the life sciences and pharmaceutical industries to perform the billions of tests necessary to extract medically valuable information from advances in genomics and proteomics. Illumina's technology will have applicability across a wide variety of industries beyond life sciences and pharmaceuticals, including agriculture, food,



Illumina's BeadArray<sup>™</sup> platform  
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chemicals and petrochemicals.

"Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995: this release may contain forward-looking statements that involve risks and uncertainties. Among the important factors which could cause actual results to differ materially from those in the forward-looking statements are Illumina's ability to fully develop its BeadArray technologies for genotyping services, the Company's ability to develop and deploy new applications for its platform technology, and other factors detailed in the Company's filings with the Securities and Exchange Commission including its recent filings on Forms 10-K and 10-Q or in information disclosed in public conference calls, the date and time of which are released beforehand. Illumina disclaims any intent or obligation to update these forward-looking statements beyond the date of this release.

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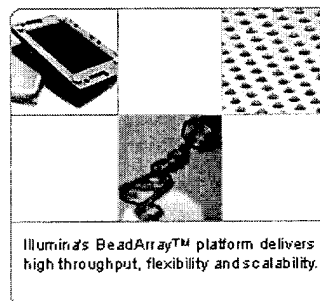
### Illumina Signs Genotyping Services Agreement with Investigators at Boston University

#### *SNP Scoring Service to Leverage Illumina's BeadArray(TM) Platform Technology*

SAN DIEGO, CALIFORNIA, January 28, 2002 - Illumina, Inc. announced today that it has signed a commercial agreement with investigators at Boston University Medical Center to provide single nucleotide polymorphism (SNP) genotyping services for a large-scale research project on preterm birth. Under the terms of the agreement, Illumina will use its BeadArray (TM) technology to "score" a set of SNPs thought to be associated with preterm birth. Illumina will also design SNP assays for the SNP loci provided by the investigators. Further details about the agreement were not disclosed.

"We are pleased that investigators at Boston University Medical Center have decided to leverage the power and cost-effectiveness of our BeadArray technology," stated Jay Flatley, Illumina President and CEO. "Investigators at Boston University Medical Center are conducting leading-edge research to understand environmental and genetic determinants of preterm birth, which is the leading cause of infant mortality and morbidity," continued Flatley. "We look forward to continued collaborations with investigators at Boston University Medical Center and other organizations to speed the analysis and lower the cost of genotyping."

Illumina (Nasdaq: ILMN; [www.illumina.com](http://www.illumina.com)) is developing next-generation tools that will permit large-scale analysis of genetic variation and function. The Company's proprietary BeadArray technology will provide the throughput, cost effectiveness and flexibility necessary to enable researchers in the life sciences and pharmaceutical industries to perform the billions of tests necessary to



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extract medically valuable information from advances in genomics. Illumina's technology will have applicability across a wide variety of industries beyond life sciences and pharmaceuticals, including agriculture, food, chemicals and petrochemicals.

"Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995: this release may contain forward-looking statements that involve risks and uncertainties. Among the important factors which could cause actual results to differ materially from those in the forward-looking statements are Illumina's ability to fully develop its BeadArray technologies, the Company's ability to develop and deploy new genomics applications for its platform technology, and other factors detailed in the Company's filings with the Securities and Exchange Commission including its recent filings on Forms 10-K and 10-Q or in information disclosed in public conference calls, the date and time of which are released beforehand. Illumina disclaims any intent or obligation to update these forward-looking statements beyond the date of this release.

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## Press Release

03/OX/02

19th March 2002

### **ILLUMINA AND OXAGEN TO COLLABORATE ON FINE MAPPING OF SNP LOCI IN GENETIC LINKAGE REGIONS**

**Illumina's BeadArray™ Technology to Enable Detailed Exploration of Linkage Regions;**

**Oxagen to Add Potential New Targets to Discovery Pipeline**

**SAN DIEGO, CALIFORNIA (USA) and ABINGDON, ENGLAND-** March 19, 2002 -

Illumina, Inc. (Nasdaq: ILMN) and Oxagen Limited, a private clinical genomics company, announced today that they have signed a collaborative, commercial agreement to generate detailed maps of single nucleotide polymorphism (SNP) clusters in defined chromosomal regions. Under the terms of the agreement, Oxagen will provide a collection of SNP loci within linkage regions together with samples from their extensive library of family collection material and information. Illumina will use its BeadArray technology to design functional assays for the SNPs provided and generate several million overall genotype calls from the sample set. Oxagen will retain rights to all genes and novel associations discovered as a result of the study. Further details about the agreement were not disclosed.

Jay Flatley, Illumina President & Chief Executive Officer, noted "Oxagen is taking a systematic, genome-wide approach to understanding the molecular basis of disease. Dr Nicholls and his team have built a large, proprietary collection of family samples and data, which represent a powerful resource for identifying and validating disease-causing genes. We're looking forward to our relationship with Oxagen, and we're confident that our genotyping capability will provide valuable information that paves the way for the identification of disease genes."

Dr. Trevor Nicholls, Oxagen Chief Executive Officer, commented "Oxagen has now created an exceptionally strong base of knowledge in relation to linkage regions relevant to the diseases we are studying. Illumina's BeadArray platform will give us the sample throughput and accuracy we need to extract the maximum information from our valuable samples. Equally important, Illumina's technology is driving down genotyping costs and making feasible large-scale studies like this one. We're very pleased about our collaboration with Illumina and expect that it will allow Oxagen to accelerate its development of improved therapeutic approaches and diagnostic tests."

### **Notes To Editors**

#### **About Illumina**

Illumina ([www.illumina.com](http://www.illumina.com)) is developing next-generation tools that permit large-scale analysis of genetic variation and function. The Company's proprietary BeadArray™ technology provides the throughput, cost effectiveness and flexibility necessary to enable researchers in the life sciences and pharmaceutical industries to perform the billions of tests necessary to extract medically valuable information from advances in genomics. Illumina's technology will have applicability across a wide variety of industries beyond life sciences and pharmaceuticals, including agriculture, food, chemicals and petrochemicals.

#### **About Oxagen**

Oxagen ([www.oxagen.co.uk](http://www.oxagen.co.uk)) has rapidly established itself as a leading player in the study of complex disease genetics, conducting programs in cardiovascular disease, inflammatory





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### Illumina Signs Genotyping Service Agreement With Johns Hopkins University

#### *SNP Scoring Service to Leverage Illumina's BeadArray (TM) Platform Technology*

SAN DIEGO, CALIFORNIA, January 8, 2002 -- Illumina, Inc. announced today that it has signed a commercial agreement with Johns Hopkins Medical University, Institute of Genetic Medicine to provide single nucleotide polymorphism (SNP) genotyping services on a sample collection provided by the Institute. Under the terms of the agreement, Illumina will use its BeadArray technology to "score," or determine the frequency of specified SNPs in the sample set. Illumina will also design functional assays for most of the SNP loci provided by the Institute. Further details about the agreement were not disclosed.

"Johns Hopkins is a world leader in the research of genetic factors associated with conditions such as cleft lip and palate and isolated craniosynostosis, and we're pleased to be able to directly support their groundbreaking research activities," stated Jay Flatley, Illumina President and CEO. "Our genotyping service capacity has reached one million genotypes per day in a highly multiplexed environment, and we look forward to working collaboratively with Johns Hopkins and other organizations to speed the analysis and lower the cost of large genotyping studies."

Illumina (Nasdaq: ILMN; [www.illumina.com](http://www.illumina.com)) is developing next-generation tools that will permit large-scale analysis of genetic variation and function. The Company's proprietary BeadArray<sup>®</sup> technology will provide the throughput, cost effectiveness and flexibility necessary to enable researchers in the life sciences and pharmaceutical industries to perform the billions of tests necessary to extract medically valuable information from advances in genomics. Illumina's technology will have applicability across a wide variety of industries beyond life sciences and pharmaceuticals, including agriculture, food, chemicals and petrochemicals.

Statements included in this press release that are not



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